Remarks

Claims 19-26, 28, and 30 are pending in the application. Claims 19-26, 28, and 30 are rejected. Applicants wish to thank the Examiner and the Supervisory Examiner for their willingness to discuss outstanding issues with the Applicants' Attorney on April 11, 2002. Applicants further thank the Examiner for pointing the withdrawal of previous rejections on pages 2-3 of the present Final Office Action.

I. Rejections of Claims 19-26, 28, and 30 under 35 U.S.C. §101 and §112, First Paragraph

The Examiner maintained the rejection of Claims 19-26, 28, and 30 under 35 U.S.C. §101 and §112, First Paragraph. The Examiner contends these claims are ". . . lacking utility and not . . . enabled for lack of utility" (Final Office Action, page 3) as noted in the previous office action (Paper Number 13). In particular, the Examiner alleges that an asserted utility of the present invention as a diagnostic indicator of inflammation ". . . is not substantiated by examples in the specification." (Final Office Action, page 3-4).

Applicants respectfully disagree with the Examiner's assertions. Applicants have listed several tissues and cells in which mRNA was tested (see, e.g., pages 61-62, of the specification). Applicants further point out samples which exhibited either high expression or detectable expression, as well as noting that a signal ". . . was not detected in any of the other listed samples tested." (see, e.g., page 67, lines 6-23, of the specification). From the expression pattern in tissue and cells indicative of an inflammatory state, Applicants are able to assert a credible, specific, and substantial utility that the present invention would ". . . be important in an inflammatory response . . ." (see, e.g., page 67, lines 21-23).

Applicants also direct the Examiner to page 4, lines 5-6; and page 47, lines 30-36. The specification contains an additional substantial, specific, and credible utility, e.g., the treatment of inflammatory conditions. Taken together, Applicants submit that the present invention has utility and is therefore properly

enabled.

Applicants further rely on M.P.E.P §2107.02(VI) allowing rebuttal of a utility rejection by submission of printed publications to support an asserted utility. Applicants' point out that the legal standard of proof required to be shown by the evidence submitted is that it is more likely than not that the asserted utility would be considered credible by a person of skill in the art. (In re Rinehart 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976)). In particular, Applicants submit that, as noted below, there is a reasonable correlation between the asserted therapeutic utility of the present invention, e.g., modulation of inflammatory conditions, and the evidence presented.

WO 01/40465 describes the effect of the CRSP polypeptide, which is encoded by the nucleic acids of the present invention, when added to a Mixed Lymphocyte Reaction (MLR). CRSP (known as PRO1199; SEQ ID NOs: 5 and 6, of WO 01/40465; see Attachment E) inhibited the MLR by 56.6-70% below control (see, e.g., pages 11 and 84, of WO 01/40465). The pertinent pages of the cited PCT application accompany this response.

The MLR (mixed lymphocyte reaction) is an assay that involves T cell activation through interaction with antigen presenting cells (APC). In the allogeneic MLR where the T cell and APC are from different donors, the T cell sees the APC as foreign, and responds by proliferation and production of many inflammatory cytokines including TNF, interferon-gamma and IL-2. The way T cells respond to APC in the allogeneic MLR mimics the way T cells respond to foreign antigens presented by self APC (i.e. APC from the same donor as the T cell) or even autoantigens involved in autoimmune inflammation, that are presented by self APCs to T cells (autologous MLR). Moreover, the response of T cells in inflammation is comparable to that seen in the MLR with production of a similar range of cytokines and by proliferation. It is also now clear that APC found in sites of inflammation such as the joint in rheumatoid arthritis are the most efficient at driving T cells in the MLR. Thus, the MLR is believed to be a good measure of the early stages of inflammation involving initial T cell-APC interactions that leads to pro-inflammatory cytokine production and development of inflammation and tissue damage (see, e.g., Waalen, et al. (1987) Scand. J.

Immunol. 26:525-533, Abstract only).

Applicant submit two background articles which describe the inflammatory process of Graft versus Host Disease (GVHD) and the use of the MLR to as an accepted measure the start of this inflammatory process (see, e.g., Thomas, et al. (eds) (1999) Hematopoietic Cell Transplantation, Blackwell Science, Inc., Malden, MA, pp. 305-315; Boussiotis, et al. (2001) Blood 97:565-571).

Taken with the expression of CRSP in inflamed tissues, noted above, Applicants believe that a reasonable correlation between the asserted utility of CRSP to modulate inflammatory processes and its ability to inhibit an MLR has been established. Furthermore, a person having ordinary skill in the art would more likely than not find the asserted utility to be credible, substantial and specific. As such, the present invention is also fully enabled.

In view of the foregoing, Applicants submit that the rejection of Claims 19-26, 28, and 30 under 35 U.S.C. §101 and §112, first paragraph, is overcome. Withdrawal of this rejection is respectfully requested.

Conclusion

Applicants' current response is believed to be a complete reply to all the outstanding issues of the Final Office Action. Further, the present response is a bona fide effort to place the application in condition for allowance or in better form for appeal. Accordingly, Applicants respectfully request reconsideration and passage of the amended claims to allowance at the earliest possible convenience. Should the Examiner deem allowance inappropriate at this time, Applicants respectfully request an interview be granted with the undersigned to consider any issues.

Respectfully submitted,

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Enclosures:

(A) International Application WO 01/40465 A2, cover pages, pages 10, 11, 81-84, Fig. 6;
(B) Abstract of Waalen, et al. (1987) Scan. J. Immunol. 26:525-533;
(C) Thomas, et al. (eds) (1999) Hematopoietic Cell Transplantation, Blackwell Science, Inc., Malden, MA, pp. 305-315;
(D) Boussiotis, et al. (2001) Blood 97:565-571; and
(E) Sequence Alignment of PRO1199 (SEQ ID NO: 6 of WO 01/40465) vs CRSP (SEQ ID NO: 2 of USSN 09/099,898).